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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/960,315	09/24/2001	Robert W. Wannemacher	12694/P66821US2 (RIID99-2	6514

7590 08/12/2004

Office of the Staff Judge Advocate
U.S Army Medical Research and Materiel Command
ATTN: MCMR-JA (Ms. Elizabeth Arwine)
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Fort Detrick, MD 21702-5012

EXAMINER	
VANDERVEGT, FRANCOIS P	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 08/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/960,315	WANNEMACHER ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09242004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of U.S. Application Serial Number 09/523,271; which claims the benefit of the filing date of provisional application 60/124,283.

Claims 1-16 and 28-39 were previously canceled.

New claims 40-46 were previously added.

Claims 17-27 and 40-46 are currently pending and are the subject of examination in the present Office Action.

Applicant's Request for Interview

In the response filed May 12, 2004 Applicant requested an interview if the outstanding issues were not resolved by the response. However, in view of the new grounds of rejection presented in this Office Action, the request for interview is presently denied. However, after Applicant has had time to review the new grounds of rejection presented, Applicant is invited to again request an interview to discuss the outstanding grounds of rejection.

1. In view of Applicant's amendment and response filed May 12, 2004, the following grounds of rejection are maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 19-20, 26-27 and 41 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It was previously stated: "Claims 19, 26 and 41 each recite the limitation that the "deglycosylated ricin A-chain is incompletely deglycosylated." This limitation is not disclosed by the specification or claims as originally filed. The specification teaches only that the chemical deglycosylation of ricin A-chain can yield a level of deglycosylation that is dependent upon the length of time that Ricin A-chain is incubated with the deglycosylating agent (page 7, line 17 to page 8, line 5 for example), the specification does not disclose that the level of deglycosylation was a controlled variable in any of the examples or

disclosed embodiments of the invention. Rather, the specification discloses that deglycosylated ricin A chain can be produced by molecular methods recombinantly produced (non-glycosylated) ricin A-chain can be used in the practice of the disclosed embodiments (page 8, line 28 to page 9, line 34, for example). Accordingly, the recitation constitutes new matter and must be removed."

Applicant's arguments filed May 12, 2004 have been fully considered but they are not persuasive. Applicant acknowledges that that the specification does not specifically recite the term "incomplete," but asserts that the term has written descriptive support because the "provided procedures can result in destruction of about 50% of mannose residues" and that 50% is "incomplete." However, it is respectfully submitted that 10, 15, 20, 85, 90, 95 and 99% are also incomplete and under different conditions, chemical treatment results in more complete or less complete deglycosylation. The instant specification describes only a single condition of chemical glycosylation resulting in a single level of ricin deglycosylation. This single example is not considered to be descriptive of the entire genus of methods of chemical deglycosylation, nor is it descriptive of "incompletely deglycosylated" in general. The specification is only descriptive of the destruction of "about 50% of the mannose and most fructose residues present on the RTA, whereas the N-acetylglucosamine and most of the xylose residues are unaffected" at pages 7-8 of the specification, for example.

3. **For examination purposes with respect to the prior art, the following is noted:**

It is noted that claims 17, 18, 25-27 and 42 recite that the deglycosylated ricin A-chain is "chemically deglycosylated." However, the specification discloses only that in chemically deglycosylated ricin A-chain, the level of deglycosylation is dependent upon the length of time that Ricin A-chain is incubated with the deglycosylating agent (page 7, line 17 to page 8, line 5 for example). Accordingly the definition of chemically deglycosylated ricin A-chain includes any degree of deglycosylation of the ricin A-chain up to and including complete lack of mannose and fructose residues and "deglycosylated ricin A chain" is interpreted to include any ricin A chain lacking glycosylation. The specification further discloses on page 8, line 28-29, for example, that deglycosylated ricin A chain can be produced by molecular methods. It was well known in the art at the time the invention was made that recombinant expression in bacterial systems results in proteins which lack glycosylation. For example, Wawrzynczak et al. (Int. J. Cancer [1991] 47:130-135; U on form PTO-892) discloses that recombinantly produced ricin A chain is a form of deglycosylated ricin A chain (page 132, last sentence first partial paragraph). Accordingly, there is no structural difference between what is encompassed by the recitation of "chemically deglycosylated" ricin A-chain and recombinant ricin A-chain. When a claim recites using an old composition or structure (e.g. deglycosylated ricin A chain) and the use is directed to a result or

property of that composition or structure (e.g., immunogenicity), then the claim is anticipated. See MPEP 2112.02.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 17, 21-25, 40, 42 and 44-46 stand rejected under 35 U.S.C. 102(b) as anticipated by U.S. Patent No. 5,453,271 to Lemley et al (A on form PTO-892, of record).

It was previously stated: "The '271 patent teaches a vaccine against ricin toxin (see entire reference). In particular, the '271 patent claims a method of immunizing a mammal against the effects of aerosol ricin toxin by administering a composition comprising an antigenic effective amount of (i.e., immunogenic) ricin A chain (RTA) in a pharmaceutically acceptable carrier (see especially claim 1). The'271 patent teaches that recombinant RTA can be used in the methods of the invention, including RTA produced in *E. coli* (which is a deglycosylated ricin A chain; column 4, lines 27-30 in particular). Accordingly, the'271 patent teaches and claims a vaccine against ricin intoxication in the form of an immunogenic composition of deglycosylated RTA in a pharmaceutically acceptable carrier. The inclusion of adjuvants in this composition is also taught (column 2, line 20)[claims 24 and 46]. Furthermore, the '271 patent teaches a dosage of 5μg per mouse (column 4, line 1), which is within the recited range of 0.1 - 10 μg per 20-25 grams body weight of the subject [claim 22] and three injections at two week intervals [claims 25, 44 and 45].

While the '271 patent is silent regarding the titer of antibodies to RTA as determined by ELISA [claims 17, 18 and 21-24], silence about a property does not necessarily constitute its absence. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that there is a difference between the materials, i.e., that the claims are directed to new materials and that such a difference would have been considered unexpected by one of ordinary skill in the art, that is, the claimed subject matter, if new, is unobvious. In the absence of evidence to the contrary, the burden is on the Applicant to prove that the claimed materials are different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

The prior art teaching anticipates the claimed invention."

Applicant argues that the reference is not anticipatory because the recombinant ricin of the '271 patent is made by bacteria and therefore have no glycosylation at all. Applicant contends that the chemically deglycosylated ricin molecules of the instant specification are not completely deglycosylated, arguing therefore that the claims are not commensurate with the teachings of the '271 patent. However, Applicant has disclosed only a single chemical treatment of ricin that removes about 50% of the mannose residues. Applicant has not provided any reason to believe that other types of chemical deglycosylation

will not completely deglycosylate ricin A chain. The claims do not recite the chemical used to deglycosylate the ricin A chain and therefore read upon all chemicals, including those that may completely deglycosylate ricin A chain, in which case the "chemically deglycosylated" ricin A chain would be identical to the recombinant ricin A chain of the '271 patent.

5. **The following represent new grounds of objection and rejection. Accordingly, this Office Action is made NON-FINAL.**

Specification

6. The disclosure is objected to because of the following informalities:

Line 73 of page 7 through line 5 of page 8 recite that the carbohydrate moieties of the ricin A chain comprise "fructose." However, the carbohydrate moieties on ricin A chain are mannose, fucose, xylose and N-acetylglucosamine (see Thorpe et al [1985]; AV on form PTO-1449).

Applicant should check the remainder of the specification for similar errors.

Appropriate correction is required. Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 18 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 is ambiguous and unclear in that it is dependent upon a canceled claim. Claim 18 should be amended to be dependent upon claim 17.

Claim 27 is indefinite in the recitation of "fructose," a carbohydrate moiety that ricin A chain does not contain. The carbohydrate moieties on ricin A chain are mannose, fucose, xylose and N-acetylglucosamine (see Thorpe et al [1985]; AV on form PTO-1449).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 17-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Thorpe et al (Eur. J. Biochem. [1985] 147:197-206; AV on form PTO-1449).

Applicant's claimed method consists of a single step, which is the administration an amount of chemically deglycosylated ricin A chain. The recitation in the claim of inducing a particular titer of anti-ricin antibodies is merely a characterization of the result of practicing the method and does not limit the method itself.

Thorpe teaches the deglycosylation of ricin A chain with sodium metaperiiodate and cyanoborohydride at a pH of 3.5 at 4°C (page 198, second column in particular). Thorpe teaches that the level of deglycosylation was dependent upon the incubation time and a maximum of 13 out of the total 18 mannose residues were destroyed (Abstract in particular). Thorpe teaches the administration of 20 μg/kg to rat subjects (Table 3 in particular). While Thorpe is silent regarding the production of ricin-reactive antibodies in the treated subject, Thorpe teaches administration of ricin A chain that has been incompletely deglycosylated in the same manner as that disclosed in the instant specification (page 7, line 17 to page 8, line 5 for example) within the claimed range of administration. Accordingly, the production of antibodies to ricin is inherent to the method of incompletely deglycosylated ricin A chain administration taught by Thorpe. The prior art teaching anticipates the claimed invention.

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
February 2, 2004

PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
8/9/04